

REMARKS

In the present communication, Claims 1, 2, 7, 9, 10, 14, and 17 have been amended and Claims 51-52 have been added. Claims 9, 10, 16, and 17 were previously withdrawn. As such, Claims 1-8, 13-15, and 51-52 are currently pending and under examination. The Examiner's rejections are as follows:

- I) Claims 1-3, 6-8, and 13-15 were rejected under 35 U.S.C. 103(a) as allegedly unpatentable over Yoshida et al. and Mahadevappa et al.;
- II) Claims 4 and 5 were rejected under 35 U.S.C. 103(a) as allegedly unpatentable over Yoshida et al., Mahadevappa et al., and Fulton et al.;
- III) Claims 1-3, 6, 7, and 13-15 were rejected under 35 U.S.C. 103(a) as allegedly unpatentable over Lebed et al. and Wang et al.; and
- IV) Claim 8 was rejected under 35 U.S.C. 103(a) as allegedly unpatentable over Lebed et al., Wang et al., and Allen et al.

I-II. Rejections Based on the Yoshida et al. Reference

The Examiner rejected Claims 1-3, 6-8, and 13-15 under 35 U.S.C. 103(a) as allegedly unpatentable over Yoshida et al. and Mahadevappa et al. (Office Action, page 3) and rejected Claims 4 and 5 over Yoshida et al., Mahadevappa et al., and Fulton et al. (Office Action, page 5). Applicants respectfully disagree with these rejections and submit that no *prima facie* case of obviousness has been established.

As part of this rejection, the Examiner cites the 54 TCR V-beta and V-alpha *specific* probes in Table 2 of Yoshida as allegedly teaching "random nucleic acid molecules." (Office Action, page 4). Applicants respectfully submit that the 54 *specific* probes are not random as they are specific, and therefore fail to teach the use of random nucleic acid sequences. None of the other references make up for this lack of teaching in Yoshida et al. Applicants further note that the claims have been amended to recite a population of random nucleic acid molecules or unselected express sequence tags (which is described in the Examples, for example, at page 17, line 20). The 54 specific primers of Yoshida et al. also are not unselected express sequence tags, and therefore do not teach this element of the claims. None of the other cited references make up for this lack of teaching. As such, Applicants submit that this rejection should be withdrawn.

Regardless of the lack of *prima facie* case of obviousness, in order to expedite the prosecution of the present application, without acquiescing to the Examiner's rejection, while reserving the right to prosecute the original or similar claims in the future, Applicants have amended the claims. In particular, Claim 1 has been amended in a number of ways. For example, Claim 1 now recites:

a standard curve generated by hybridizing said population of nucleic acid molecules with two or more different samples each containing a known number of variant nucleic acid molecules, wherein said standard curve provides the frequency of hybridization versus the number of variants present;

Claim 1 has also been amended to recite determining "the frequency of hybridization," as well as:

d) comparing said frequency of hybridization to said standard curve in order to quantify the amount lymphocyte diversity in said subject.

Support for these amendments is found throughout the specification including, for example, page 2, line 29 - page 3, line 1; page 13, lines 24-30; page 17, lines 27 - page 18, line 2; page 18, lines 16-20; Examples 1-6; Figure 1A; and Figure 1B.

Applicants respectfully submit that the amended claims further distinguish over the cited references. For example, none of the cited reference teach the use of such a standard curve, or the use of a standard curve to generate a *quantitative* assessment of lymphocyte diversity (e.g., none of the cited references attempt to quantify lymphocyte diversity). As such, Applicants submit that the amendments to the claims are additional reasons that these rejections should be withdrawn.

III-IV. Rejections Based on the Lebed et al. Reference

The Examiner rejected Claims 1-3, 6, 7, and 13-15 under 35 U.S.C. 103(a) as allegedly unpatentable over Lebed et al. and Wang et al. (Office Action, page 6). The Examiner also rejected Claim 8 under 35 U.S.C. 103(a) as allegedly unpatentable over Lebed et al., Wang et al., and Allen et al. (Office Action, page 8). Applicants respectfully disagree with these rejections and submit that they are moot in view of the claim amendments discussed above as the cited art does not teach all the limitations of the amended claims. For example, none of the cited references teach the use of a standard curve or the use of a standard curve to generate a

quantitative assessment of lymphocyte diversity. As such, Applicants submit that these rejections should be withdrawn.

CONCLUSION

Should the Examiner believe that a telephone interview would aid in the prosecution of this application, Applicants encourage the Examiner to call the undersigned at 608-218-6900.

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